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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/036,988	12/31/2001	Roger L. Papke	UF-293	5315

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EXAMINER	
KWON, BRIAN YONG S	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 02/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/036,988	PAPKE, ROGER L.	
	Examiner	Art Unit	
	Brian S Kwon	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 December 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-5 and 7-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-5 and 7-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Summary of Action

I. The rejection of claims 1-10 under 35 USC 112, first paragraph, will not be maintained in light of the amendment.

II. The rejection of claims 1-10 under 35 USC 103(a) will be maintained for the reason of the record.

Status of Application

1. By Amendment filed December 01, 2003, Claims 2, 6 and 11-20 have been cancelled and Claims 1, 3-5, 9 and 10 have been amended. Claims 1, 3-5 and 7-10 are currently pending for prosecution on the merits.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

2. Claims 1, 3-5 and 7-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Crooks et al. (US 5616707) in view of Newhouse et al. (Society of Biological Psychiatry, (Feb. 2001), 49:268-278).

This rejection is analogous to the original rejection.

Response to Arguments

3. Applicant's arguments and submitted Declaration filed December 01, 2003 have been fully considered but they are not persuasive.

Applicant's argument takes position that "Although metanicotine was once proposed to be a potential drug for the treatment of AD (as indicated in the Crooks et al. patent), recent studies have suggested that the appropriate molecular target for this indication is in fact the alpha7 receptor...Thus, based upon what was known of metanicotine's activity from the scientific literature at the time the subject patent application was filed, there would be no motivation to administer metanicotine for treatment of Alzheimer's disease (AD), by itself or in combination with other recited compounds". This argument is not persuasive. Regardless of whatever the underlying mechanism involved in pathophysiology of Alzheimer's disease (AD), the usefulness of metanicotine for the treatment of Alzheimer's disease was well known to the skill artisan at the time of the invention was made (Bencherif et al. (US 6218383) and (WO 2001082978); "Radiosynthesis and PET studies of [11C]RJR-2403, a nicotinic agonist", Studenov et al., Journal of Labelled Compounds & Radiopharmaceuticals, 2001, 44(6), 425-436). Therefore, one having ordinary skill in the art would have been motivated to combine the references and make such modification to arrive at the claimed invention. One skill artisan would

have been motivated to make the modification such that the combination of metanicotine and ABT-428 would provide enhanced therapeutic effect in treating Alzheimer's disease while providing less adverse effects that may be resulted from activation of receptors associated with undesirable side effects. The fact that new underlying pharmacological mechanism of, metanicotine was discovered is not considered patentably distinctive over the prior art which are directed to the same therapeutic utility (for the treatment of Alzheimer's disease). Especially, in view of the state art where the underlying cause of Alzheimer's disease is still not known and there are no known diagnostic tool, cure and single effective treatment for Alzheimer's disease, the skill artisan would be motivated to administer for the treatment of Alzheimer's disease (AD), alone or in combination with the other recited compounds.

Applicant's argument takes position that "As demonstrated by the experimental data in the subject application, treatment with metanicotine actually decreased the residual inhibition otherwise exhibited by mixed agonists-antagonists....Thus, the co-administration of metanicotine and the recited compounds has a synergistic effect and this interaction is unexpected in view of the activities of the individual compounds". This argument is not persuasive. Unlike applicant's argument, Example 5 and Figures 6A and 6B of the instant patent application and the Papke (2002) publication fail to show the alleged synergistic effects. It is not clear from reading Figures 6A and 6B that the recovery after DMXB plus TC-2403 (metanicotine) is greater than the additive effect of each individual compound (DMXB or TC-2403) since no experimental data on TC-2403 alone is present. Without applicant's showing the recovery after each individual DMXB and TC-2403 in comparison with the recovery after DMXB plus TC-2403, the examiner cannot make proper determination whether applicant's combination achieves greater

(synergistic) effect than the expected results (the additive effect of each individual compound) or not. As discussed in preceding comments, in absence of showing the side-by-side comparison data showing the alleged synergistic effect, the examiner maintains that the claimed invention is obvious to the skill artisan. It is obvious to combine two compositions each of which is taught by prior art to be useful for same purpose; idea of combining them flows logically from their having been individually taught in the prior art.

Conclusion

4. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (571) 272-0581. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marianne Seidel, can be reached on (571) 273-0584. The fax number for this Group is (703) 872-9306.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Brian Kwon
Patent Examiner
AU 1614

ZOHREH FAY
PRIMARY EXAMINER
GROUP 1600